Appendix 4: SPF Study Clinical Report

SUN PROTECTION FACTOR (SPF) DETERMINATION

TKL STUDY NO. PB801000

CONDUCTED FOR:

The Procter & Gamble Company
Sharon Woods Technical Center
11511 Reed Hartman Highway
Cincinnati, Ohio 45241

Attention: J. Frank Nash, PhD

DATE OF DRAFT REPORT:

August 4, 2000
Revised September 1, 2000

TABLE OF CONTENTS

TITLE OF STUDY

Sun Protection Factor (SPF) Determination of Sunscreen Products Under Static Conditions

SPONSOR

The Procter & Gamble Company
Sharon Woods Technical Center
11511 Reed Hartman Highway
Cincinnati, Ohio 45241

Attention: J. Frank Nash, PhD

STUDY MATERIALS

Code B	MF# SWS316-074
Code C	MF# SWS316-076
Code D	MF# SWS316-078
Code E	MF# SWS316-094
Code F	MF# SWS316-096
Code G	MF# SWS316-095
Code I	MF# BCS541-116
Code J	MF# BCS541-118

DATE STUDY INITIATED

April 12, 2000

DATE STUDY COMPLETED

June 20, 2000

DATE OF DRAFT REPORT

August 4, 2000

INVESTIGATIVE PERSONNEL

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CLINICAL SITE

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4 Forest Avenue
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STATEMENT OF QUALITY ASSURANCE

All data and supporting documentation for this study have been audited by the TKL Quality Assurance Department and found to be accurate, complete and in compliance with the requirements of the protocol and TKL's Standard Operating Procedures. This report has been reviewed and accurately reflects all aspects of the conduct of the study.

All clinical research studies are performed by TKL Research, Inc. in accordance with federal regulations and proposed guidelines for good clinical practices which include:

21 CFR Part 312, Investigational New Drug Application

21 CFR Part 50, Protection of Human Subjects

21 CFR Part 56, Institutional Review Boards

_____ _____

Senior Quality Assurance Associate Date

SUMMARY

Product Codes B, C, D, E, F, G, I, and J, were evaluated for Sun Protection Factor (SPF) determination under standard sunscreen study conditions. Fifty-six subjects completed the study, some of whom evaluated more than one product. An 8% Homosalate solution served as a control.

Under the conditions employed in this study, the following Sun Protection Factors were obtained:

PRODUCT IDENTIFICATION[2]	EST. SPF	SPF/STD. DEVIATION[1]	NUMBER OF SUBJECTS
B	19-20	21.07 ± 2.61	14
C	19-25	22.96 ± 3.21	14
D	19-25	21.42 ± 3.31	14
E	5-11	9.05 ± 1.90	14
F	5-11	11.37 ± 1.52	14
G	5-11	10.09 ± 1.76	14
I	5-11	9.97 ± 1.04	14
J	22-28	24.68 ± 4.52	14

1 Calculation according to FDA OTC Review Panel for Sunscreen Products, Proposed Monograph, published in the Federal Register, August 25, 1978 (Vol. 43, No. 166).

2 Subjects were assigned into product group numbers due to administrative purposes (the computer SPF program used could not enter all the products in one file) and the sponsors breakdown of the products into two groups. Subjects testing product B, C, D, E, F and G, were assigned group A. The sponsor requested that products from group A begin testing first. Group A subjects were given enrollment numbers with no suffix. Subjects testing products I and J, received enrollment numbers ending with the letter B. Eight subjects tested products from groups A and B receiving enrollment numbers from both groups.

1.0 INTRODUCTION

1.1 OBJECTIVE

The objective of the study was to determine the sun protection factor of a sunscreen product under static conditions.

1.2 RATIONALE

Sunscreens are topically applied substances which protect the skin from adverse effects of excessive exposure to solar radiation (or equivalent sources of light, e.g., sunlamps). The amount of protection afforded varies greatly with the nature of the sunscreen; the physical activity engaged in while wearing the sunscreen; the amount of sun exposure; and the type of light blocked out by the screen (e.g., "burning rays" - UVB, or "tanning rays" - UVA).

Most sunscreens are chemical sunscreens that contain one or more light absorbing chemicals incorporated into a cream, lotion, or gel-type vehicle. Once applied to the skin, these chemicals are usually effective as an invisible thin film. Physical sunscreens are formulations which contain substances that primarily reflect and/or scatter radiation. Manufacturers of sunscreen formulations label their products according to the sun protection factor (SPF). The SPF is defined as follows:

$$\text{SPF} = \frac{\text{Minimal Erythema Dose (MED) of sunscreen protected skin}}{\text{Minimal Erythema Dose (MED) of unprotected skin}}$$

The MED is the time required to produce a minimal erythemal reaction using a standardized ultraviolet light source that emits UVB (290 - 320 nm) as all or part of its emission spectrum. The higher the SPF of a sunscreen, the longer an individual can be exposed to light without experiencing an adverse reaction such as sunburn.

1.3 BACKGROUND

Eight products were submitted for evaluation on a study group of no less than 4 volunteer subjects. On the basis of information provided by the Sponsor, these products were considered reasonably safe for evaluation on human subjects.

2.0 STUDY MATERIALS

2.1 STORAGE, HANDLING, AND DOCUMENTATION OF STUDY MATERIALS

Upon arrival of the materials used in this study at TKL Research, Inc., receipt was documented in a general log book which serves as a permanent record of the receipt, storage, and disposition of all study materials. A sample of the study material was reserved and will be stored for a period of six months. At the conclusion of the clinical study, the remaining study materials was discarded or returned to the Sponsor and the disposition documented in the log book. All information regarding the receipt, storage and disposition of the study materials was also recorded on a Clinical Material Record form (see Appendix II) which is incorporated in this study report. All study materials are kept in a locked product storage room accessible to clinical staff members only.

2.2 NATURE OF STUDY MATERIALS

Product Identification	:	Code B MF# SWS316-074
Description	:	off-white lotion
Quantity Provided	:	2 x 80 g
Amount Applied	:	0.12 g/60 cm^2
Expiration Date	:	02/01/01

Product Identification	:	Code C MF# SWS316-076
Description	:	off-white lotion
Quantity Provided	:	2 x 80 g
Amount Applied	:	0.12 g/60 cm^2
Expiration Date	:	02/01/01

Product Identification	:	Code D MF# SWS316-078
Description	:	off-white lotion
Quantity Provided	:	2 x 80 g
Amount Applied	:	0.12 g/60 cm^2
Expiration Date	:	02/01/01

Product Identification	:	Code E MF# SWS316-094
Description	:	white lotion
Quantity Provided	:	2 x 80 g
Amount Applied	:	0.12 g/60 cm^2
Expiration Date	:	02/01/01

Product Identification	:	Code F MF# SWS316-096
Description	:	white lotion
Quantity Provided	:	2 x 80 g
Amount Applied	:	0.12 g/60 cm^2
Expiration Date	:	02/01/01

Product Identification	:	Code G MF# SWS316-095
Description	:	white lotion
Quantity Provided	:	2 x 80 g
Amount Applied	:	0.12 g/60 cm^2
Expiration Date	:	02/01/01

Product Identification	:	Code I MF# BCS541-116
Description	:	white lotion
Quantity Provided	:	2 x 80 g
Amount Applied	:	0.12 g/60 cm^2
Expiration Date	:	02/01/01

Product Identification	:	Code J MF# BCS541-118
Description	:	yellowish liquid
Quantity Provided	:	2 x 80 g
Amount Applied	:	0.12 g/60 cm^2
Expiration Date	:	02/01/01

3.0 EXPERIMENTAL DESIGN

3.1 STUDY GROUP SELECTION

A minimum of 20 subjects were enrolled in the study.

3.1.1 Inclusion Criteria

1. Individuals 18 years of age or older.

2. Individuals with Fitpatrick Skin Types I, II, or III and uniformly-colored skin on the lower thoracic area of the back which would allowed a discernment erythema.

3. Individuals free of any systemic or dermatologic disorder which, in the opinion of the investigative personnel, would interfere with the study results.

4. Individuals who completed a photo study Medical Screening form, as well as a Medical/Personal History form.

5. Individuals who read, understood and signed an informed consent agreement.

3.1.2 Exclusion Criteria

1. Individuals with any visible skin disease excessive hair, blemishes, tan or uneven pigmentation at the study site which, in the opinion of the investigative personnel would interfere with the study results.

2. Individuals taking any anti-inflammatory medication which, in the opinion of the investigative personnel, might interfere with the study results.

3. Individuals taking medication suspected of causing photobiological reactions (e.g., tetracyclines, thiazides).

4. Individuals with psoriasis and/or active atopic dermatitis/ eczema.

5. Females who were pregnant, planned to become pregnant during the study, or were breast-feeding a child.

6. Individuals with diabetes.

7. Individuals who were currently under steroidal treatment for asthma, non-steroidal treatment is acceptable (e.g., Proventil inhaler).

8. Individuals with cataracts.

9. Individuals with a history of skin cancer.

10. Individuals with a history of hepatitis.

11. Individuals with a known sensitivity to cosmetics, skin care products or topical drugs as related to the material being evaluated.

3.1.3 Informed Consent

A properly executed informed consent document in compliance with FDA regulations (21 CFR 50) was obtained from each subject prior to entering the study. The signed informed consent is maintained in the study file. In addition, the subject was provided with a copy of the informed consent. A sample of the consent agreement is included as Appendix IV.

3.2 DESCRIPTION OF STUDY

3.2.1 Study Design

The design is in accordance with the Final Monograph, 21 CFR Parts 310, 352, 700, 740, "Sunscreen Drug Products for Over-the-Counter Human Use" (Federal Register vol. 64, number 98 pages 27666-27693, May 21, 1999).

3.2.2 Light Source

A Xenon Arc Solar Simulator (150W) was used which had a continuous emission spectrum in the UVA and UVB range (290-400 nanometers). The output was monitored at the beginning and periodically throughout each irradiation day using the Robertson-Berger Meter to assure uniform intensity.

3.2.3 Standard Sunscreen

To assure the uniform evaluation of sunscreen products, a standard sunscreen was used concomitantly in the study procedure. This control product is an 8% homosalate preparation with an SPF value of approximately 4.0.

3.2.4 Outline of Study Procedures

Subjects reported to the test site for Visit 1 and were screened for inclusion/exclusion criteria. Those subjects qualifying were tested to determine their MED (minimal erythema dose) for unprotected skin, as outlined below. The following day (Visit 2) the subjects returned and if their MEDs fulfilled the requirements, they were tested with product and returned the next day for their final visit.

Treatment Assignment- The test sites were located on the subject's back between the beltline and the shoulder blade and lateral to the mid-line. The treatment assignment divided the subject's back into a series of test sites. Each test site was subdivided into seven subsites and each subsite was a minimum of one square centimeter. Individual test sites were randomly assigned to either, No treatment- determination for MED of unprotected skin, Test Formulation, or 8% Homosalate Reference.

Ultraviolet Radiation Source- A 150-Watt Berger Xenon Arc Solar Simulator (Solar Light Co., Philadelphia, PA) was used as the ultraviolet radiation source in this study. A 1mm WG-320 and 1mm UG-11 filter was used to provide a continuous emission spectrum in the UVA and UVB range (290-400nanometers).

Energy Measurements- The ultraviolet radiation output was monitored at the beginning and periodically throughout each irradiation day using a Robertson-Berger UV meter to assure uniform intensity.

Determination of MED of Unprotected Skin (MED[US])- A series of exposures was administered to five 1 cm^2 sites on the unprotected skin on each subject's back to determine each individual's inherent minimal erythema dose (MED [US]), (Visit 1). The anticipated MED was estimated from the skin type (I, II or III) of the individual and the irradiation times calculated were based on the required energy output of the Xenon lamp to achieve a minimal erythema reaction. Each of the five sites was irradiated for exposure times that differ by a factor of 1.25, i.e., each irradiated site receives 25% more exposure than the previous site. The series of doses were designed to determine the smallest dose of energy that produces redness reaching the borders of the exposure site 22 to 24 hours post exposure for each series of exposures. The goal was to have:

a) at least one site without erythema
b) minimally perceptible erythema and
c) one or more sites with light to moderate erythema

This procedure was repeated at treatment and ultraviolet exposure (Visit 2), and then evaluated on the last day.

Determination of MED of Static SPF- Within each treatment area, a series of ultraviolet radiation exposures was administered to seven 1 cm^2 protected subsites to determine the MED of the protected skin (MED[PS]). The doses selected shall consist of a geometric series of five exposures, where the middle exposure is placed to yield the expected SPF plus two other exposures placed symmetrically around the middle exposure. These exposures are calculated from the guidelines in the Final Monograph.

The SPF value of the test article sunscreen was then calculated from the dose of ultraviolet radiation required to produce the MED of the protected skin (MED[PS]) and from the dose of the ultraviolet radiation required to produce the MED of the unprotected skin (MED[US]) Therefore:

$$SPF = \frac{(MED[PS])}{(MED[US])}$$

3.3 Definition of Terms

MED (Minimal Erythema Dose)

The time of light exposure necessary to produce a minimal perceptible erythema (redness) on the skin, discernible 22 to 24 hours later.

SPF (Sun Protection Factor)

The ultraviolet energy required to produce an MED on protected skin, divided by the ultraviolet energy required to produce an MED on unprotected skin.

3.4 SPF Evaluations and Statistical Analysis

Following challenge of individual subsites with ultraviolet radiation, evaluations were made for each of the following parameters under normal laboratory illumination. Immediately after challenge individual subsites were examined for the presence or absence of immediate darkening (tan, gray or purple in color), immediate reddening and immediate heat response.

Twenty-two to twenty-four hours after challenge with ultraviolet radiation each subsite was examined at the same position as when the test site was irradiated. A subsite chosen within each test site determines the smallest dose of energy that produces redness to the borders of the exposure site.

The sites were evaluated to determine the MED with either a tungsten light bulb or a warm white florescent light bulb that provides illumination of the test sites. All test sites were evaluated using the following scale:

ERYTHEMA	
-	No reaction
?	Minimal or doubtful erythema, barely perceptible compared to surrounding skin
+	Mild, but definite erythema
++	Moderate erythema
+++	Marked/severe erythema

EDEMA

**	Mild, but definite edema
***	Definite edema with erosion/vesiculation

SPECIAL NOTATIONS

Hr	Hyperpigmentation
V	Vesiculation
P	Papular response
pv	Papulo-vesicular response
D	Damage to epidermis: oozing, crusting and/or superficial erosions
I	Itching
S	Spreading of reaction beyond study site (i.e., reaction where no product comes in contact with the skin)
f	Follicular irritation with or without pustule formation (folliculitis)
X	Subject absent

Calculation of SPF and PCD

The Label SPF and PCD category following the 1999 final monograph could not be determined for this study due to the requirement of calculating the mean SPF from a minimum of 20 evaluable subjects.

3.4.1 Study Flow Chart

DAY	ACTIVITIES
1	Obtained informed consent; completed medical screening form; conducted UV irradiation for MED determination.
2	Determined MED; calculated UV exposure times; irradiated study product site, control product[1] site and untreated site for second MED determination.
3	Evaluated all sites; calculated SPF.

[1] To assure the uniform evaluation of sunscreen products, a standard sunscreen was used concomitantly in the study procedure. This control product is an eight percent (8%) homosalate preparation (prepared by Cosmetech Laboratories, Inc.).

3.5 REJECTION OF STUDY DATA

There could be two reasons for rejection of study data.

1. Sometimes the exposure either fails to elicit an MED response on either the treated or unprotected skin sites or elicits responses at all five irradiated sites. In either event, that study is a technical failure and must be discarded. If the subject reacts to one or more exposures on the unprotected control site, but not the treated site, then a minimal estimate can be obtained. However, this estimate would not be used in assessing the Mean of the SPF values.

2. The response on the treated sites is randomly absent, which indicates the product was not spread evenly. Therefore, no assessment of protection is possible.

4.0 DATA SUMMARY

See Tables B through J - Appendix I.

5.0 PROTOCOL

See Protocol – Appendix V.

6.0 DOCUMENTATION AND RETENTION OF DATA

The case report forms were designed to identify each subject by subject number and/or subject entry number and, where appropriate, subject's initials, the product(s) evaluated and the reactions observed. Originals or copies of all case report forms, source documents, IRB documents (if required), correspondence, study reports, etc. will be kept on hard-copy file for a minimum of five years from completion of the study. Storage is maintained either at the TKL Research, Inc. facility in a secured room accessible only to TKL employees, or at an offsite location which provides a secure environment with burglar/fire alarm systems, camera detection and controlled temperature and humidity. Documentation will be available for the Sponsor's review on the premises of TKL Research, Inc.

7.0 RESULTS & DISCUSSION

Product Codes B, C, D, E, F, G, I, and J, were evaluated for Sun Protection Factor (SPF) determination under standard sunscreen study conditions. A total of 56 subjects between the ages of 28 and 71 were enrolled and completed SPF evaluation of the study products and the 8% Homosalate control (See Demographics - Appendix III).

Under the conditions employed in this study, the following Sun Protection Factors and associated values were obtained:

PRODUCT IDENTIFICATION[2]	EST. SPF	SPF/STD. DEVIATION[1]	NUMBER OF SUBJECTS
B	19-20	21.07 ± 2.61	14
C	19-25	22.96 ± 3.21	14
D	19-25	21.42 ± 3.31	14
E	5-11	9.05 ± 1.90	14
F	5-11	11.37 ± 1.52	14
G	5-11	10.09 ± 1.76	14
I	5-11	9.97 ± 1.04	14
J	22-28	24.68 ± 4.52	14

[1] Calculation according to FDA OTC Review Panel for Sunscreen Products, Proposed Monograph, published in the Federal Register, August 25, 1978 (Vol. 43, No. 166).

[2] Subjects were assigned into product group numbers due to administrative purposes (the computer SPF program used could not enter all products in one file) and the sponsors breakdown of the products into two groups. Subjects testing product B, C, D, E, F, and G, were assigned group A. The sponsor requested that products from group A begin testing first. Group A subjects were given enrollment numbers with no suffix. Subjects testing products I, and J, received enrollment numbers ending with the letter B. Eight subjects tested products from groups A and B receiving enrollment numbers from both groups.

9.0 SIGNATURES

Maureen Damstra, BA
Certified Clinical Research Coordinator

Date

Alan H. Greeenspan, MD
Principal Investigator

Date

Robert C. Reardon, PhD
Director of Operations

Date

APPENDIX I

TABLES

PROCTER & GAMBLE Product SPF TKL Study No.: PB801000

Subject No.	B MF# SWS316-074	CONTROL HMS 8%
1	18.57	4.00
3	18.81	3.52
6	20.21	5.00
9	23.51	5.00
13	20.21	4.00
15	23.24	4.00
16	23.55	4.41
17	25.30	6.25
18	23.21	4.00
31	19.11	4.40
32	19.11	4.40
36	23.51	4.40
39	20.24	5.00
40	16.39	3.20
Mean:	**21.07**	**4.40**
STD:	**2.61**	**0.75**
STD Error:	**0.70**	**0.20**
5% of Mean:	**1.05**	**0.22**
N =:	**14**	**14**

PROCTER & GAMBLE | Product SPF | TKL Study No.: PB801000

Subject No.	C MF# SWS316-076	CONTROL HMS 8%
2	29.01	4.40
4	23.51	6.25
8	27.60	5.00
10	24.00	4.40
11	19.20	3.53
19	23.21	4.00
20	25.30	4.00
29	25.27	3.59
31	23.51	4.40
32	20.49	4.40
34	22.00	5.00
38	20.49	4.40
39	20.24	5.00
40	17.60	3.20
Mean:	**22.96**	**4.40**
STD:	**3.21**	**0.77**
STD Error:	**0.86**	**0.21**
5% of Mean:	**1.15**	**0.22**
N =:	**14**	**14**

PROCTER & GAMBLE Product SPF TKL Study No.: PB801000

Subject No.	D MF# SWS316-078	CONTROL HMS 8%
5	19.11	5.00
7	15.05	4.00
9	29.01	5.00
12	18.84	5.00
21	17.60	5.00
22	23.24	5.00
23	23.24	5.00
24	20.45	4.00
25	23.24	5.00
26	22.00	6.25
27	22.00	5.00
28	23.55	4.00
29	22.00	3.59
30	20.49	5.00
Mean:	**21.42**	**4.77**
STD:	**3.31**	**0.67**
STD Error:	**0.88**	**0.18**
5% of Mean:	**1.07**	**0.24**
N =:	**14**	**14**

PROCTER & GAMBLE Product SPF TKL Study No.: PB801000

Subject No.	E_MF# SWS316-094	CONTROL HMS 8%
1	7.36	4.00
4	8.70	6.25
6	7.70	5.00
8	8.70	5.00
13	7.70	4.00
15	5.30	4.00
16	11.50	4.41
17	11.50	6.25
18	7.68	4.00
31	8.70	4.40
32	11.50	4.40
35	9.60	5.00
37	11.50	5.00
39	9.20	5.00
Mean:	**9.05**	**4.77**
STD:	**1.90**	**0.76**
STD Error:	**0.51**	**0.20**
5% of Mean:	**0.45**	**0.24**
N =:	**14**	**14**

PROCTER & GAMBLE | Product SPF | TKL Study No.: PB801000

Subject No.	F MF#SWS 316-096	CONTROL HMS 8%
4	8.70	6.25
10	10.88	4.40
11	9.63	3.53
14	10.39	5.02
19	11.50	4.00
20	10.88	4.00
21	11.50	5.00
22	11.50	5.00
23	11.50	5.00
24	14.38	4.00
25	11.50	5.00
27	14.38	5.00
28	10.94	4.00
40	11.50	3.20
Mean:	**11.37**	**4.53**
STD:	**1.52**	**0.79**
STD Error:	**0.41**	**0.21**
5% of Mean:	**0.57**	**0.23**
N =:	**14**	**14**

PROCTER & GAMBLE | Product SPF | TKL Study No.: PB801000

Subject No.	G MF# SWS316-095	CONTROL HMS 8%
3	9.20	3.52
5	9.60	5.00
8	12.94	5.00
10	9.79	4.40
21	8.66	5.00
22	7.88	5.00
23	7.88	5.00
24	10.83	4.00
25	10.35	5.00
28	12.94	4.00
29	12.94	3.59
30	9.79	5.00
33	9.79	4.00
41	8.64	5.00
Mean:	**10.09**	**4.54**
STD:	**1.76**	**0.59**
STD Error:	**0.47**	**0.16**
5% of Mean:	**0.50**	**0.23**
N =:	**14**	**14**

PROCTER & GAMBLE Product SPF TKL Study No.: B801000

Subject No.	I MF# BCS541-116	CONTROL HMS 8%
1	9.20	5.00
10	11.50	5.00
11	9.63	4.41
12	9.20	4.00
13	9.20	3.53
15	9.63	4.41
16	9.63	3.19
17	9.60	4.00
18	11.50	5.00
19	9.60	5.00
20	8.70	4.40
21	11.50	5.00
22	11.50	4.40
23	9.20	5.00
Mean:	**9.97**	**4.45**
STD:	**1.04**	**0.60**
STD Error:	**0.28**	**0.16**
5% of Mean:	**0.50**	**0.22**
N =:	**14**	**14**

PROCTER & GAMBLE Product SPF TKL Study No.: B801000

Subject No.	J MF# BCS541-118	CONTROL HMS 8%
2	21.68	4.00
4	23.28	4.40
5	23.28	4.40
6	35.94	5.50
12	17.34	4.00
15	28.71	4.41
16	25.00	3.19
17	21.72	4.00
18	21.72	5.00
19	28.75	5.00
20	23.28	4.40
21	26.72	5.00
22	26.72	4.40
23	21.38	5.00
Mean:	**24.68**	**4.48**
STD:	**4.52**	**0.59**
STD Error:	**1.21**	**0.16**
5% of Mean:	**1.23**	**0.22**
N =:	**14**	**14**

APPENDIX II

CLINICAL MATERIAL RECORD

TKL RESEARCH, INC. 4 FOREST AVENUE PARAMUS, NJ 07652

CLINICAL MATERIAL RECORD

Study No.:PB801000

PRODUCT ID CODE	PRODUCT DESCRIPTION	EXPIRATION DATE	RECEIPT	ADDITIONAL RECEIPT	STORAGE CONDITIONS *see code below	RETAINED SAMPLE
CODE B MF# SWS316-074	OFF WHITE LOTION	02/01/01	DATE: 3/31/2000 AMOUNT: 2 X 80g	N/A	A	N/A
CODE C MF# SWS316-076	OFF WHITE LOTION	02/01/01	DATE: 3/31/2000 AMOUNT: 2 X 80g	N/A	A	N/A
CODE D MF# SWS316-078	OFF WHITE LOTION	02/01/01	DATE: 3/31/2000 AMOUNT: 2 X 80g	N/A	A	N/A
CODE E MF# SWS316-094	WHITE LOTION	02/01/01	DATE: 3/31/2000 AMOUNT: 2 X 80g	N/A	A	N/A
CODE F MF# SWS316-096	WHITE LOTION	02/01/01	DATE: 3/31/2000 AMOUNT: 2 X 80g	N/A	A	N/A
CODE G MF# SWS316-095	WHITE LOTION	02/01/01	DATE: 3/31/2000 AMOUNT: 2 X 80g	N/A	A	N/A
CODE I MF# BCS541-116	WHITE LOTION	02/01/01	DATE: 3/31/2000 AMOUNT: 2 X 80g	N/A	A	N/A
CODE J MF# BCS541-118	YELLOWISH LIQUID	02/01/01	DATE: 3/31/2000 AMOUNT: 2 X 80g	N/A	A	N/A

DISPOSITION DATE: To be discarded 8/28/00 CARRIER: _____

DISPOSITION: ❻ RETURNED ❻ DISCARDED

SPONSOR: The Procter & Gamble Company

RECEIPT RECORDED BY: TMT

DISPOSITION RECORDED BY: _____

LOG BOOK PAGE NUMBER: 135

*STORAGE CONDITIONS: A = AMBIENT (Room Temperature) CONDITIONS W = WARMER (Temp. Req._____) R = REFRIGERATED (4-8°C) F = FROZEN (Temp. Req._____)

O = OTHER (EXPLAIN): _____

STORAGE INFORMATION: An aliquot of the sample or a full (pre-packaged) product or device will be retained for a period of six months.

APPENDIX III

DEMOGRAPHICS

KEY:

F = Female
M = Male

DEMOGRAPHICS

Entry No.*	Subject No.	Sex	Race	Age
01	40689	M	OTHER	46
02	07100	F	WHITE	68
03	16040	F	WHITE	52
04	49183	F	WHITE	39
05	41588	M	WHITE	45
06	62006	M	WHITE	40
07	66551	F	WHITE	42
08	14267	M	WHITE	65
09	12549	F	WHITE	42
10	07041	F	WHITE	71
11	49797	F	WHITE	42
13	14964	F	WHITE	28
14	16024	F	WHITE	63
15	11398	F	WHITE	51
16	41269	M	WHITE	41
17	13933	F	WHITE	46
18	49663	F	WHITE	63
19	16894	F	WHITE	59
20	16896	F	WHITE	41
21	19486	F	WHITE	46
22	53008	F	WHITE	51
23	12896	F	WHITE	40
24	19186	F	WHITE	39
25	53792	F	WHITE	35
26	42220	F	WHITE	44
27	55066	F	WHITE	49
28	15696	F	WHITE	39
29	17721	F	WHITE	44
30	57564	F	WHITE	33
31	49517	F	WHITE	68
32	50895	F	WHITE	41
39	20052	F	WHITE	53
40	40818	F	WHITE	40
02B	09396	F	WHITE	53
03B	53469	F	WHITE	43
04B	17689	F	WHITE	57
05B	46346	F	WHITE	38
06B	40567	F	WHITE	53
07B	15080	M	WHITE	36
08B	40775	F	WHITE	42
09B	15324	F	WHITE	42
10B	09913	F	WHITE	61
11B	13253	F	WHITE	64

DEMOGRAPHICS

Entry No.*	Subject No.	Sex	Race	Age
12B	60871	F	WHITE	43
13B	16801	F	WHITE	65
14B	49184	F	WHITE	39
15B	42351	F	WHITE	67
16B	42487	M	WHITE	44
12/ 01B	12624	F	WHITE	51
17/ 33B	49253	F	WHITE	35
18/ 34B	41738	F	WHITE	38
19/ 35B	17600	F	WHITE	43
20/ 36B	59054	F	WHITE	49
21/ 37B	15083	F	WHITE	58
22/ 38B	60416	F	WHITE	33
23/ 41B	55980	F	WHITE	60

DISTRIBUTION OF AGES

Under 18	: n =	0
18 to 25	: n =	0
26 to 35	: n =	5
36 to 45	: n =	25
46 to 55	: n =	12
56 to 65	: n =	10
Over 65	: n =	4
Total	: n =	56

Mean Age: 47.9

Age range for the study: 28 to 71

[3] Subjects were assigned into product group numbers due to administrative purposes (the computer SPF program used could not enter 12 products in one file) and the sponsors breakdown of the products into two groups. Subjects testing product B, C, D, E, F, G and H were assigned group A. The sponsor requested that products from group A begin testing first. Group A subjects were given enrollment numbers with no suffix. Subjects testing products I, J, K, L and M received enrollment numbers ending with the letter B. Eight subjects tested products from groups A and B receiving enrollment numbers from both groups.

APPENDIX IV

INFORMED CONSENT DOCUMENT

INFORMED CONSENT
ULTRAVIOLET A FACTOR DETERMINATION

STUDY NO.:PB840400

PURPOSE: The purpose of this research is to determine the ability of sunscreen products to prevent the sun-tanning or sun burning reaction caused by the ultraviolet A (UVA) portion of sunlight when contact with the skin is followed by UVA light exposure and to determine the UVA protection factor of the sunscreen products.

ELIGIBILITY: A member of the research staff will explain the study to you and you will be asked to read and sign this consent form. You will be asked to complete a form about your medical history and a member of the research staff will examine your back.

Only healthy volunteers with normal skin will be allowed to participate in this study.

While you are in this study, please inform the clinical staff if you have any change in your medical health, as well as any medications you are taking or applying to your skin. This includes medication ordered for you by another doctor, or drugs you buy from a store without a prescription. You may not participate in any other study while you are a subject in this study.

If you are a female of childbearing potential (i.e., not surgically sterile or have not experienced menopause), you must agree to prevent pregnancy throughout this three-day study by using an accepted form of birth control [e.g., oral contraceptive pill, IUD, condom/diaphragm with spermicide, abstinence (no sexual relations)]. Pregnant women and nursing women are excluded from this study. Women should not become pregnant or breast-feed an infant while participating in this study to prevent any unknown risk to the unborn or nursing child.

STUDY PROCEDURE: Upon qualifying, you will be expected to discontinue use of all creams, lotions, moisturizers, or any other skin products on your lower back and to protect your back from sun exposure for the duration of the study. You will take part in a study that extends over a 3 day period. A minimum of 10 subjects will participate in this research study.

A small portion of your lower back will be exposed to UVA light from a solar simulator (a lamp whose light is similar to that of sunlight but more intense). You will be exposed at six (6) sites which are circular and have a diameter of one (1) centimeter (less than 2 inches). This is done to see the least amount of light it takes to produce a sun tan reaction on the skin. The exposure will be approximately 15 minutes. You will return the next day to have the sites evaluated.

On day two up to five other areas of your back (each about the size of a business card) will have sunscreen products applied and exposed to UVA from a solar simulator. The exposures will be approximately 14-60 minutes at each site. You may wish to bring reading material for this visit.

The following day you will return to the study center to have the study sites evaluated for a tanning or redness response. You will be required to remain at TKL Research for approximately 10 minutes.

POSSIBLE DISCOMFORTS OR RISKS: There may be some irritation at the study sites similar to a sunburn and/or a suntan, or in rare cases, a reaction at the study sites where the test formulation touches the skin, characterized by varying degrees of redness, swelling, blistering, temporary stinging, burning sensation, itching, eczema (inflammation, scaling and itching), petechiae (small pinpoint non-raised red dots), dryness, hyperpigmentation (darkening of the skin) and/or peeling. Occasionally, a reaction may result in localized lightening or darkening of the skin, which may persist for several weeks or months before fading. The Study Coordinator and/or Investigator (the Study doctor) may withdraw you from this study for reasons of, but not limited to, a severe reaction, an illness, or your failure to follow directions.

You will be told of any significant new findings developed during the course of this study which may relate to your

INFORMED CONSENT
ULTRAVIOLET A FACTOR DETERMINATION

STUDY NO.:PB840400

OMPENSATION: In the event that any injury should occur to you as a direct result of the test materials and your participation in this study, appropriate medical treatment will be provided by TKL Research, Inc. paid by the Sponsor (the company conducting this study). If such reactions occur, TKL personnel should be contacted immediately at (201) 587-0505 including nights and weekends.

VOLUNTARY PARTICIPATION: Participation in this study is voluntary. You may refuse to participate or withdraw at any time without prejudice or loss of benefits that you would otherwise be entitled. There are no anticipated costs to you that may result from your participation in this study.

FINANCIAL INCENTIVE: You will be paid $70.00 upon completion of all phases of this study. If, in the judgment of the investigating personnel, it is best to discontinue your participation in this study, due to an adverse experience or severe reaction, you will be paid in full for your participation. If you are dismissed for refusal to obey rules or follow instructions you will not be paid. If you drop out on your own accord for personal reasons beyond your control you will be paid proportionately.

BENEFITS/ ALTERNATIVES: There is no personal benefit to participating in this study. Not participating in this study is your alternative.

RELEASE OF MEDICAL RECORDS AND CONFIDENTIALITY: Unless required by law, only the investigator (study doctor), the sponsor (the company conducting this study), employees of TKL Research, Inc. and representatives of the Essex Institutional Review Board (a committee that has reviewed this research project to help ensure that the rights and welfare of the participants are protected and that the study is carried out in an ethical manner) and government regulatory agencies will have access to confidential data which identifies you by name. You will not be identified by name in any reports or publications resulting from the study.

WHOM TO CONTACT: If you have additional questions about this research during the course of the study or in the event of a research-related injury or any other problems, call Alan H. Greenspan, MD, Principal Investigator, or Maureen Damstra, Clinical Research Coordinator, at (201) 587-0505. You may contact the Essex Institutional Review Board, 121 Main St., Lebanon, NJ 08833, (908) 236-7735 if you have a question about your rights as a research subject.

CONSENT

I have read and understand this consent form. I have had an opportunity to ask questions and my questions have been answered. I voluntarily consent to participate. I will be given a copy of this signed consent form. By signing this form I have not given up any of my legal rights which I may have in the case of negligence or other legal fault of anyone who is involved in this study that I would otherwise have as a research subject.

SIGNATURE

SUBJECT:	_____	_____	_____
	Signature	Please Print	Date
WITNESS:	_____	_____	_____
	Signature	Please Print	Date

Entry No:_____

APPENDIX V

PROTOCOL

PROTOCOL FOR

DETERMINATION OF STATIC UVA PROTECTION FACTORS (PFA)

TKL-8401-M

SUBMITTED BY:

The Procter & Gamble Company
Sharon Woods Technical Center
11511 Reed Hartman Highway
Cincinnati, OH 45241-9974

SUBMITTED BY:

TKL Research, Inc.
4 Forest Avenue
Paramus, NJ 07652

Date

March 29, 2000

TABLE OF CONTENTS

Page No.

1.0 TITLE

Determination of Static UVA Protection Factors (PFA)

2.0 OBJECTIVE

The objective of the study is to determine the static UVA Protection Factor (PFA) for Sunscreen formulas.

3.0 STUDY DESIGN

This will be a controlled, randomized study. Subjects entered into the study will have their initials entered sequentially on the Subject Assignment Sheet. The randomization of the application of the study products to the areas of the subject's back will be indicated on this sheet.

3.1 STUDY POPULATION

Each subject is expected to participate in the study for 3 days.

3.1.1 Inclusion Criteria

1. Individuals 18-65 years old will be enrolled into the study only after it is determined that each belongs to skin type I, II, or III as defined in the proposed monograph for SUNSCREEN DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN DRUGS, Federal Register of August 25, 1978 (43FR38206-38269).

2. Individuals free of any systemic or dermatologic disorder which, in the opinion of the investigative personnel, will interfere with the study results or increase the risk of adverse events.

3. Individuals who complete a photo study Medical Screening form, as well as a Medical/Personal History form.

4. Individuals who read, understand and sign an informed consent agreement.

3.1.2 Exclusion Criteria

1. Medical history not consistent with good general health.

2. History of recent (topical or systemic) use of medication, cosmetic, soap, or fragrance formulations known to product abnormal sunlight responses.

3. History of severe abnormal responses to sunlight.

4. Individuals with any visible skin disease, excessive hair, blemished, tan or uneven pigmentation at the study site which, in the opinion of the investigative personnel will interfere with the study results.

5. History of chronic use of high doses of antihistamine or anti-inflammatory medications (e.g., aspirin, ibuprofen or corticosteroids) or current use of any antihistamine, NSAID or prescription anti-inflammatory drugs.

6. Individuals taking medication suspected of causing photobiological reactions (e.g. tetracyclines, thiazides).

7. Individuals with psoriasis and/or active atopic dermatitis /eczema.

8. Females who are pregnant, plan to become pregnant during the study, or are breast-feeding a child.

9. Individuals with diabetes, Addison's disease or thyroid conditions.

10. Individuals who are currently under steroidal treatment for astham, non steroidal treatment is acceptable (e.g., Proventil inhaler).

11. Individuals with cataracts.

12. Individuals with a history of skin cancer.

13. Individuals with a history of hepatitis.

14. Individuals with a known sensitivity to cosmentics, skin care products or topical drugs as related to product(s) being evaluated.

4.0 PROCEDURE

4.1 PRE-STUDY

Before being entered into the study, the subjects will be pre-screened by the investigator for the criteria indicated in the Subject Selection section. Only subjects who meet the requirements of this section, have signed an informed consent according to 21 CFR, Part 50 and have given an appropriate medical history will be entered into this study.

4.2 LIGHT SOURCE

The source of radiation will be a Xenon arc solar simulator having a continuous emission spectrum in the UVA (320 to 380 nm) region with less than 1% of its total energy contributed by wavelengths below 320 nm. The lamp will be filtered with a WG335 filter, 3mm in thickness or equivalent. There will be less than 2% of erythemal effectiveness of the source contributed from wavelengths lower than 320 nm, and no more than 10% of the total output of the lamp will be visible and infrared radiation. The maximum intensity at the point of the skin exposure must be less than 150 mW/cm^2 total irradiance, as measured by a calibrated thermopile.

4.3 MINIMAL RESPONSE DOSE (MRD) DETERMINATION

On Day 1 of the study, a minimal response dose (MRD) for unprotected skin will be determined for each subject by irradiating 5 one-centimeter subsites on the lower back. The dose interval selected for the irradiation of the subsites shall be a geometric series wherein each exposure dose interval is 25% greater than the previous exposure. This geometric series is represented by 1.25 X n where n is the previous exposure dose.

For subjects of unknown sensitivity, the dose series will be in the range of 10 to $31J/cm^2$. For subjects with predetermined UVA MRD values, the dose series will be centered around the previously determined MRD.

After the exposure is completed, all immediate responses will be recorded. These include immediate darkening or tanning, immediate erythema, whealing, edema or flaring at the irradiation site. Subjects exhibiting the last three responses will be disqualified from the study procedures.

After the immediate responses are recorded, the subjects will be instructed to shield the exposed areas from further UV exposure. Sixteen to 24 hours after the UV exposure, the 5 subsites will be graded using the scale indicated in the Clinical Measurements section. The subsite with the lowest exposure dose showing a minimally perceptible tanning or erythema response will be selected as the MRD. The unprotected MRD will be reconfirmed on the day the test products are evalauted.

4.4 PFA DETERMINATION

1. Application of Test Products: Using a permanent marker, each subject will have six 50cm^2 test areas drawn on the back between the beltline and the shoulder blades and lateral to the midline. Five of four test areas will be for the study products and the remaining one will be used for the MRD. Following the randomization indicated on the Subject Assignment Sheet, 100 mg of Sunscreen formula will be applied to the appropriate test area and spread over the entire area using a finger cot.

   In the same manner, 100 mg of Sunscreen formulas will be applied to the designated test areas. The test areas are allowed to dry for 20 minutes. During this period, the subjects should be instructed not to touch their backs against any surface.

2. Irradiation of the Static PFA Test Areas: While the test areas are drying, the solar simulator exposure doses required for Sunscreen formulas will be calculated based on the MRD of the subject and the expected PFA value of the sunscreen.

   Each 50cm^2 test are will contain 5 subsites that will be irradiated. The dose intervals selected for the subsites shall be a geometric series in which each exposure doe (subsite) is 25% greater than the previous exposure dose (1.25 x n). For example, if the subject's unprotected MRD is 10 J/cm^2 and the expected PFA of the sunscreen is 2, then the central exposure interval (third subsite) will be 10 X 2 or 20 J/cm^2, respectively. At the completion of the exposure at each subsite.

   Sixteen to 24 hours after irradiation, all subsites in the test areas will be graded for responses using the scale indicted in the Clinical Measurements section and the PFA values will be determined.

5.0 CLINICAL MEASUREMENT

Sixteen to 24 hours after irradiation, all subsites in the test areas will be graded for responses using the scale indicated below. The person performing the grading will be unaware of the identity of the treatments applied to the test areas.

0 = No reaction
0.5 = Minimal tanning or erythema, barely perceptible
1 = Light brown or red color with definite borders
1.5 = Medium brown or red, well-defined
2 = Dark brown or red with edema

The lowest dose subsite showing a minimally perceptible response (0.5) will be selected as the MRD value. The PFA of the sunscreen is the ratio of the exposure dose for the protected MRD divided by the dose for the unprotected MRD (PFA = protected MRD/unprotected MRD).

6.0 MATERIALS

6.1 ADMINISTRATION

On the day of study, a research technician will weigh the test articles and then apply by manually and uniformly spreading the test article over a 50 cm^2 area at a dose of 2mg/cm^2. A waiting period of at least 15 minutes is required before proceeding with the ultraviolet exposure.

6.2 SUPPLIES

All study materials will be shipped by the sponsor will explicit instructions for handing and storage. Upon receipt all products will be logged in and stored in a secure area.

7.0 ADVERSE EVENTS

An adverse event is defined as an occurrence of a new symptom(s) of a medical nature during use of the study material whether or not considered related to the study material, e.g., headache, influenza, broken bones, fever, nausea, etc. All clinical adverse events, whether observed by the clinical staff or by the subject and whether or not thought to be study-related, are considered adverse events and will be recorded on an Adverse Event form. Assessment of severity and causality will be based on definitions found on the Adverse Events report form. A separate Adverse Event Form will be completed for each adverse event reported.

Serious adverse events will be reported to the Sponsor within 24 hours of the Investigator's knowledge of the event. Clinical personnel will contact the Sponsor as soon as the adverse event is identified.

It is understood that the Investigator will stop application of the study material at any time the Investigator feels the subject's condition so indicates.

8.0 CONCOMITANT MEDICATIONS

The use of concomitant medications will be allowed only if it had been detrmined that the medication will not in any way interfere with the study results.

9.0 INTERCURRENT ILLNESS

Any intercurrent illness occurring during the course of this study should be recorded in the case report form.

10. DISCONTINUATION FROM THE STUDY

Patients must be discontinued from the study for the following reasons:

Serious or intolerable adverse experiences at least possible related to study treatment in the judgment of the Investigator.

Requirement of prohibited concomitant medication as outlied in the ecxlusion criteria and concomitant medications.

Non-compliance by the subject.

Withdrawal of consent by the subject.

For all subjects discontinued from the study, the reason for the discontinuation will be documented in the Case Report Form.

11.0 STATISTICAL ANALYSIS

Statistical Analysis – The following calculations for each of the products will be performed:

Mean Static PFA
Standard Deviation
Standard Error
5% of the Mean

Rejection of Data – Test data will be rejected if the exposure series fails to elicit an MRD on treated or unprotected skin sited. Test data will be rejected if the responses on the treated sited are randomly absent, or if the subject was noncompliant.

12.0 STUDY MONITORING AND RECORD RETENTION

12.1 QUALITY ASSURANCE

All data and supporting documentation for this study will be audited by the TKL Quality Assurance Department and deemed to be accurate, complete and in compliance with all requirements of the protocol and TKL's Standard Operating Procedures.

12.2 FINAL REPORT

At the conclusion of the study, the Sponsor will receive a final report including background data, study materials, tables of raw data and data summary, and an interpretation with discussion, if required, of results.

12.3 AGREEMENT WITH PROTOCOL

TKL Research, Inc. agrees to conduct the title study as provided in this protocol, in accordance with all government regulations and to make no changes without prior notification to the Sponsor except where a modification is deemed necessary to eliminate or reduce risk to human subjects.

SUBMITTED BY:

_____ _____

Maureen Damstra
Clinical Research Coordinator
TKL Research, Inc.

Date

APPROVED BY:

_____ _____

J Frank Nash, Ph. D.,
Senior Scientist
The Procter & Gamble Company

Date

APPENDIX IV

INFORMED CONSENT DOCUMENT

INFORMED CONSENT

SUN PROTECTION FACTOR (SPF) DETERMINATION (2-day)

STUDY NO. : PB801000

PURPOSE

The purpose of this research is to determine the ability of study materials to prevent a sunburn reaction when contact with the skin is followed by an ultraviolet light exposure.

STUDY MATERIALS

The study samples are sun screen products and are intended to come into contact with human skin. Some of these materials may be irritating under certain conditions, but the degree of irritation is not expected to be greater than that described below.

STUDY DURATION

The study will extend over a two (2)-day period and will involve a minimum of 5 participants.

PROCEDURE:

DAY ONE: At a previous visit the lowest amount of ultraviolet (UV) light that will give you a minimal sunburn reaction (called a minimal erythema dose or MED) was determined. This was done by exposing a small portion of your lower back to UV light from a solar simulator (a lamp whose light is similar to that of sunlight but more intense) at five sites that are circular and have a diameter of 1 centimeter (less than half an inch). This previous MED will be used to determine the amount of exposure to UV light you will receive during this study.

Six study sites each 50 cm^2 (slightly larger than a business card) will be chosen on your back. Four study materials will be applied to your back in the chosen areas and exposed to light from a solar simulator. The next site will have a control product (a standard sunscreen) applied and exposed to light from a solar simulator. The final area of untreated skin will be exposed to light from a solar simulator to determine the MED of unprotected skin. This visit will last approximately 1-1&1/2 hours. You will return to TKL Research, Inc. the following day, in 22 to 24 hours, at your appointed time. Your back must be protected from sun exposure during the 2-day study period.

DAY TWO: All sites will be evaluated.

If you are a female of childbearing potential (i.e., not surgically sterile or have not experienced menopause), you must agree to prevent pregnancy throughout this study by using an accepted form of birth control (e.g., oral contraceptive pill, IUD, condom/diaphragm with spermicide, abstinence [no sexual relations])

If you are nursing a child, you will not be permitted to participate in this study. Pregnancy and nursing are prohibited to prevent any unforeseen risks to an unborn or nursing child.

POTENTIAL RISKS

There may be some irritation at the study site or increased pigmentation (like a suntan) or in rare cases, a reaction at the study sites where the product touches the skin, characterized by varying degrees of redness, swelling, burning sensation and/or itching. In extremely rare cases, some blistering may occur at the study site. All of these changes are rapidly reversible, although some increased pigmentation at the study site(s) may persist in an occasional individual.

For any significant reactions, which may occur as a direct result of your participation in this study, appropriate and reasonable medical treatment will be provided at no cost to you to relieve the immediate problem. Provision of such medical care is not an admission of legal liability or responsibility for the condition being treated. If such reactions occur, TKL personnel should be contacted immediately at (201) 587-0505. Extended medical care will not be provided.

INFORMED CONSENT

SUN PROTECTION FACTOR (SPF) DETERMINATION (2-day)

STUDY NO. : PB801000

POTENTIAL BENEFITS

There is no personal benefit to you other than the satisfaction of participation in a clinical research study.

WITHDRAWAL FROM STUDY

Participation in the study is voluntary and you may refuse to participate or may withdraw at any time without obligation or prejudice to you. Your participation may also be discontinued at any time without your consent by the study doctor, the Institutional Review Board (IRB, a committee that reviews studies to help ensure that the rights and welfare of the participants are protected and that the study is carried out in an ethical manner), the Food and Drug Administration (FDA), or the study sponsor (the company that makes the products being evaluated). If you fail to comply with study procedures, your participation may be terminated.

FINANCIAL INCENTIVE

You will be paid a sum of $40.00 upon completion of this study. If, in the judgment of the investigating personnel, it is best to discontinue your participation in this study due to an adverse experience or severe reaction, you will be paid in full for your participation. If you are dismissed for refusal to obey rules or follow instructions you will not be paid. If you drop out on your own accord for personal reasons beyond your control you will be paid proportionately.

CONFIDENTIALITY

Reports prepared by TKL Research will utilize statistical information only and at no time will your name be used. Your records will be kept as confidential as possible under local, state and federal laws. The study sponsor, the employees of TKL, the Food and Drug Administration and the Institutional Review Board may review the records, which may include access to names and information relating to study participants.

WHO TO CONTACT

Additional information regarding this research is available either before or during the course of this study. If you have any questions or research-related side effect or injury, you may contact Maureen Damstra, Clinical Research Coordinator, at (201) 587-0505. You may contact the Essex Institutional Review Board, 121 Main Street, Lebanon, NJ 08833, (908) 236-7735 if you have a question about your rights as a research subject.

A signed copy of this consent form will be given to you.

I have read and understand this consent form. I have had an opportunity to ask questions and my questions have been answered. I voluntarily consent to participate. By signing this form I have not given up any of my legal rights which I would otherwise have as a research subject.

ENTRY NO. _____ PRINT NAME _____ SIGNATURE _____ DATE _____

SIGNATURE OF WITNESS _____ DATE _____

INFORMED CONSENT

SUN PROTECTION FACTOR (SPF) DETERMINATION (3-day)

STUDY NO. : PB801000

PURPOSE

The purpose of this research is to determine the ability of twelve (12) study materials to prevent a sunburn reaction when contact with the skin is followed by an ultraviolet light exposure.

STUDY MATERIALS

The study samples are sunscreen products and are intended to come into contact with human skin. Some of these materials may be irritating under certain conditions, but the degree of irritation is not expected to be greater than that described below.

STUDY DURATION

The study will extend over a three (3)-day period and will involve a minimum of 5 participants.

PROCEDURE

DAY ONE (Visit 1: Approximately 10 minutes): A small portion of your lower back will be exposed to ultraviolet (UV) light from a solar simulator (a lamp whose light is similar to that of sunlight but more intense) at 5 sites that are circular in shape and have a diameter of 1 centimeter (less than half an inch). This is done to determine the lowest amount of UV light that will give you a minimal sunburn reaction (called a minimal erythema dose or MED). Your back must be protected from sun exposure during the 3-day study period. You will return to TKL Research, Inc. the following day, in 22 to 24 hours, at your appointed time.

DAY TWO: Four to five study sites each 50 cm^2 (slightly larger than a business card) will be chosen on your back. Two to three study materials will be applied to your back in the chosen area and exposed to light from a solar simulator. The next site will have a control product (a standard sunscreen) applied and exposed to light from a solar simulator. The final area of untreated skin will be exposed to light from a solar simulator to determine the MED of unprotected skin. This visit will last approximately 60-90 minutes. You will return to TKL Research, Inc. the following day, in 22 to 24 hours, at your appointed time.

DAY THREE: All sites will be evaluated.

If you are a female of childbearing potential (i.e., not surgically sterile or have not experienced menopause), you must agree to prevent pregnancy throughout this study by using an accepted form of birth control (e.g., oral contraceptive pill, IUD, condom/diaphragm with spermicide, abstinence [no sexual relations])

If you are nursing a child, you will not be permitted to participate in this study. Pregnancy and nursing are prohibited to prevent any unforeseen risks to an unborn or nursing child.

POTENTIAL RISKS

There may be some irritation at the study site or increased pigmentation (like a suntan) or in rare cases, a reaction at the study sites where the product touches the skin, characterized by varying degrees of redness, swelling, burning sensation and/or itching. In extremely rare cases, some blistering may occur at the study site. All of these changes are rapidly reversible, although some increased pigmentation at the study site(s) may persist in an occasional individual.

For any significant reactions which may occur as a direct result of your participation in this study, appropriate and reasonable medical treatment will be provided at no cost to you to relieve the immediate problem. Provision of such medical care is not an admission of legal liability or responsibility for the condition being treated. If such reactions occur, TKL personnel should be contacted immediately at (201) 587-0505. Extended medical care will not be provided.

INFORMED CONSENT

SUN PROTECTION FACTOR (SPF) DETERMINATION (3-day)

STUDY NO. : PB801000

POTENTIAL BENEFITS

There is no personal benefit to you other than the satisfaction of participation in a clinical research study.

WITHDRAWAL FROM STUDY

Participation in the study is voluntary and you may refuse to participate or may withdraw at any time without obligation or prejudice to you. Your participation may also be discontinued at any time without your consent by the study doctor, the Institutional Review Board (IRB, a committee that reviews studies to help ensure that the rights and welfare of the participants are protected and that the study is carried out in an ethical manner), the Food and Drug Administration (FDA), or the study sponsor (the company that makes the products being evaluated). If you fail to comply with study procedures, your participation may be terminated.

FINANCIAL INCENTIVE

You will be paid a sum of $50.00 upon completion of this study. If, in the judgment of the investigating personnel, it is best to discontinue your participation in this study due to an adverse experience or severe reaction, you will be paid in full for your participation. If you are dismissed for refusal to obey rules or follow instructions you will not be paid. If you drop out on your own accord for personal reasons beyond your control you will be paid proportionately.

CONFIDENTIALITY

Reports prepared by TKL Research will utilize statistical information only and at no time will your name be used. Your records will be kept as confidential as possible under local, state and federal laws. The study sponsor, the employees of TKL, the Food and Drug Administration and the Institutional Review Board may review the records, which may include access to names and information relating to study participants.

WHO TO CONTACT

Additional information regarding this research is available either before or during the course of this study. If you have any questions or research-related side effect or injury, you may contact Maureen Damstra, Clinical Research Coordinator, at (201) 587-0505. You may contact the Essex Institutional Review Board, 121 Main Street, Lebanon, NJ 08833, (908) 236-7735 if you have a question about your rights as a research subject.

A signed copy of this consent form will be given to you.

I have read and understand this consent form. I have had an opportunity to ask questions and my questions have been answered. I voluntarily consent to participate. By signing this form I have not given up any of my legal rights which I would otherwise have as a research subject.

ENTRY NO. PRINT NAME SIGNATURE DATE

SIGNATURE OF WITNESS DATE

APPENDIX V

PROTOCOL

PROTOCOL FOR

SUN PROTECTION FACTOR (SPF) DETERMINATION

TKL-8000-m-p&g

SUBMITTED TO:

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SUBMITTED BY:

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TABLE OF CONTENTS

Page No.

1.0 TITLE

Sun Protection Factor (SPF) Determination

2.0 INTRODUCTION

Sunscreens are topically applied substances which protect the skin from the adverse effects of excessive exposure to solar radiation (or equivalent sources of light, e.g., sunlamps). The amount of protection afforded varies greatly with (1) the nature of the sunscreen; (2) the physical activity engaged in while wearing the sunscreen; (3) the amount of sun exposure; and (4) the type of light blocked out by the screen (e.g., "burning rays" -UVB, or "tanning rays" - UVA).

Most sunscreens are chemical sunscreens that contain one or more light absorbing chemicals incorporated into a cream, lotion or gel-type vehicle. Once applied to the skin, these chemicals are usually effective as an invisible thin film and are cosmetically acceptable to most people.

Physical sunscreens are formulations which primarily reflect and/or scatter radiation. They are cosmetically unacceptable to many people, but may be essential for individuals with severe photosensitivity disorders. They are also useful for small, limited areas, such as the nose and lips. The manufacturers of sunscreen formulations are labeling their products according to the sun protection factor (SPF).

The MED is the time required to produce a minimal erythemal reaction using a standardized ultraviolet light source that emits UVB (290-320 nm) as all or part of its emission spectrum.

3.0 OBJECTIVE

The objective of the study is to determine the sun protection factor of a sunscreen product under static conditions.

4.0 STUDY DESIGN

4.1 Study Population

A minimum of 20 subjects will be enrolled in the study.

4.1.1 Inclusion Criteria

1. Individuals 18 years of age or older.

2. Individuals with Fizpatrick Skin Types I, II, or III and uniformly-colored skin on the lower thoracic area of the back which will allow discernment of erythema.

3. Individuals free of any systemic or dermatologic disorder which, in the opinion of the investigative personnel, will interfere with the study results.

4. Individuals who complete a photo study Medical Screening form, as well as a Medical/Personal History form.

5. Individuals who read, understand and sign an informed consent agreement.

4.1.2 Exclusion Criteria

1. Individuals with any visible skin disease, excessive hair, blemishes, tan or uneven pigmentation at the study site which, in the opinion of the investigative personnel would interfere with the study results.

2. Individuals taking any anti-inflammatory medication which, in the opinion of the investigative personnel, might interfere with the study results.

3. Individuals taking medication suspected of causing photobiological reactions (e.g., tetracyclines, thiazides).

4. Individuals with psoriasis and/or active atopic dermatitis/eczema.

5. Females who are pregnant, plan to become pregnant during the study, or are breast-feeding a child.

6. Individuals with diabetes.

7. Individuals who are currently under steroidal treatment for asthma, non-steroidal treatment is acceptable (e.g., Proventil inhaler).

8. Individuals with cataracts.

9. Individuals with a history of skin cancer.

10. Individuals with a history of hepatitis.

11. Individuals with a known sensitivity to cosmetics, skin care products or topical drugs as related to the material being evaluated.

4.2 Description of Study

4.2.1 Study Design

The design is in accordance with the Final Monograph, 21 CFR Parts 310, 352, 700, 740, "Sunscreen Drug Products for Over-the-Counter Human Use" (Federal Register vol. 64, number 98 pages 27666-27693, May 21, 1999).

4.2.2 Light Source

A Xenon Arc Solar Simulator (150W) will be used which has a continuous emission spectrum in the UVA and UVB range (290-400 nanometers). The output will be monitored at the beginning and periodically throughout each irradiation day using the Robertson-Berger Meter to assure uniform intensity.

4.2.3 Standard Sunscreen

To assure the uniform evaluation of sunscreen products, a standard sunscreen will be used concomitantly in the study procedure. This control product is an 8% homosalate preparation with an SPF value of approximately 4.0.

4.2.4 Outline of Study Procedures

Subjects will report to the test site for Visit 1 and will be screened for inclusion/exclusion criteria. Those subjects qualifying will be tested to determine their MED (minimal erythema dose) for unprotected skin, as outlined below. The following day (Visit 2) the subjects will return and if their MEDs fulfill the requirements, they will be tested with product and return the next day for their final visit.

Treatment Assignment- The test sites will be located on the subject's back between the beltline and the shoulder blade and lateral to the mid-line. The treatment assignment will divide the subject's back into a series of test sites. Each test site will be subdivided into seven subsites and each subsite will be a minimum of one square centimeter. Individual test sites will randomly assigned to either, No treatment- determination for MED of unprotected skin, Test Formulation, or 8% Homosalate Reference.

Ultraviolet Radiation Source- A 150-Watt Berger Xenon Arc Solar Simulator (Solar Light Co., Philadelphia, PA) will be used as the ultraviolet radiation source in this study. A 1mm WG-320 and 1mm UG-11 filter will be used to provide a continuous emission spectrum in the UVA and UVB range (290-400nanometers).

Energy Measurements- The ultraviolet radiation output will be monitored at the beginning and periodically throughout each irradiation day using a Robertson-Berger UV meter to assure uniform intensity.

Determination of MED of Unprotected Skin (MED(US))- A series of exposures is administered to five 1 cm^2 sites on the unprotected skin on each subject's back to determine each individual's inherent minimal erythema dose (MED (US)), (Visit 1). The anticipated MED is estimated from the skin type (I, II or III) of the individual and the irradiation times calculated are based on the required energy output of the Xenon lamp to achieve a minimal erythema reaction. Each of the five sites is irradiated for exposure times that differ by a factor of 1.25, i.e., each irradiated site receives 25% more exposure than the previous site. The series of doses are designed to determine the smallest dose of energy that produces redness reaching the borders of the exposure site 22 to 24 hours post exposure for each series of exposures. The goal is to have:

a) at least one site without erythema
b) minimally perceptible erythema and
c) one or more sites with light to moderate erythema

This procedure will be repeated at treatment and ultraviolet exposure (Visit 2), and then evaluated on the last day.

Determination of MED of Static SPF- Within each treatment area, a series of ultraviolet radiation exposures will be administered to seven 1 cm^2 protected subsites to determine the MED of the protected skin (MED(PS)). The doses selected shall consist of a geometric series of five exposures, where the middle exposure is placed to yield the expected SPF plus two other exposures placed symmetrically around the middle exposure. These exposures are calculated from the guidelines in the Final Monograph.

The SPF value of the test article sunscreen will then be calculated from the dose of ultraviolet radiation required to produce the MED of the protected skin (MED(PS)) and from the dose of the ultraviolet radiation required to produce the MED of the unprotected skin (MED(US)) Therefore:

$$SPF = \frac{(MED(PS))}{(MED(US))}$$

5.0 STUDY MATERIAL AND APPLICATION

All study samples will be supplied and shipped by the sponsor with explicit instructions for handling and storage. Upon receipt all products will be logged in and stored in a secure area. Unless otherwise directed by the Sponsor, the study material will be discarded upon completion of the study. A sample will be retained for a period of 6 months.

5.1 ADMINISTRATION

On the day of the test, a research technician will treat each assigned site with the test articles by manually and uniformly spreading the test article over a 60 cm^2 at a dose of 2mg/cm^2or 2 ul/cm^2. A waiting period of at least 15 minutes (or the time indicated on the test article label) is required before proceeding with the ultraviolet exposure. The study material will be removed from the sites after UV exposure using an alcohol prep. The test areas will be outlined with a skin marker.

6.0 SAFETY REPORTING

6.1 ADVERSE EVENTS

An adverse event is defined as an occurrence of a new symptom(s) of a medical nature during use of the study material whether or not considered related to the study material, e.g., headache, influenza, broken bones, fever, nausea, etc. All clinical adverse events, whether observed by the clinical staff or by the subject and whether or not thought to be study-related, are considered adverse events and will be recorded on an Adverse Event form. Assessment of severity and causality will be based on definitions found on the Adverse Events report form.

Serious adverse events will be reported to the Sponsor within 24 hours of the investigative personnel's knowledge of the event.

It is understood that the Investigator will stop application of the study material at any time the subject's condition so indicates.

6.2 CONCOMITANT MEDICATIONS

The use of concomitant medications will be allowed only if it had been determined that the medication will not in any way interfere with the study results.

6.3 INTERCURRENT ILLNESS

Any intercurrent illnesses occurring during the course of this study should be recorded in the case report form.

6.4 DISCONTINUATION FROM THE STUDY

Patients must be discontinued from the study for the following reasons:

Serious or intolerable adverse experiences at least possibly related to study treatment in the judgment of the Investigator.

Requirement of prohibited concomitant medication as outlined in the exclusion criteria and concomitant medications.

Non-compliance by the subject.

Withdrawal of consent by the subject.

For all subjects discontinued from the study, the reason for the discontinuation will be documented in the Case Report Form.

6.5 SPF Evaluations and Statistical Analysis

Following challenge of individual subsites with ultraviolet radiation, evaluations will be made for each of the following parameters under normal laboratory illumination. Immediately after challenge individual subsites will be examined for the presence or absence of immediate darkening (tan, gray or purple in color), immediate reddening and immediate heat response.

Twenty-two to twenty-four hours after challenge with ultraviolet radiation each subsite will be examined at the same position as when the test site was irradiated. A subsite chosen within each test site determines the smallest dose of energy that produces redness to the borders of the exposure site.

The sites will be evaluated to determine the MED with either a tungsten light bulb or a warm white florescent light bulb that provides illumination of the test sites. All test sites will be evaluated using the following scale:

ERYTHEMA	
-	No reaction
?	Minimal or doubtful erythema, barely perceptible compared to surrounding skin
+	Mild, but definite erythema
++	Moderate erythema
+++	Marked/severe erythema
EDEMA	
**	Mild, but definite edema
***	Definite edema with erosion/vesiculation
SPECIAL NOTATIONS	
Hr	Hyperpigmentation
V	Vesiculation
P	Papular response
pv	Papulo-vesicular response
D	Damage to epidermis: oozing, crusting and/or superficial erosions
I	Itching
S	Spreading of reaction beyond study site (i.e., reaction where no product comes in contact with the skin)
f	Follicular irritation with or without pustule formation (folliculitis)
X	Subject absent

Calculation of SPF and PCD - The efficacy of the sunscreen test article formulation will be determined from a test panel of no more than 25 completed subjects. The mean SPF value (x) is calculated using a minimum of 20 evaluable subjects. The standard deviation will be determined (s). The upper 5% point will be obtained from the t distribution table with n-1 degrees of freedom (t). First, A will be calculated as follows:

$$A=\frac{(t)\,(s)}{\sqrt{N}}$$

The label SPF is the largest whole number less than the mean SPF minus A.

$$\text{Label SPF} = \text{Mean SPF} - A$$

The Product Category Designation (PCD), for labeling purposes, will be assigned based on the mean SPF and PCD ranking according to the Final Monograph. Classification may be High (SPF value of 30 or above), Moderate (SPF value of 12 to 30) or Minimal (SPF value of 2 to under 12).

Rejection of Data - Test data will be rejected if the exposure series fails to elicit an MED on treated or unprotected skin sites. Test data will be rejected if the responses on the treated sites are randomly absent, or if the subject was noncompliant.

7.0 CONDUCT OF THE STUDY

7.1 ADMINISTRATION

7.1.1 Institutional Review

An appropriate Institutional Review Board (IRB) will review the protocol and all addenda for this study, if required. The IRB letter of approval will be kept on file and a copy will be provided to the Sponsor.

7.1.2 Informed Consent

A properly executed informed consent document in compliance with FDA regulations (21 CFR 50) will be obtained from each subject prior to entering the study. The signed informed consent document will be maintained in the study file and a copy given to the subject.

7.1.3 Quality Assurance

All data and supporting documentation for this study will be audited by the TKL Quality Assurance Department and deemed to be accurate, complete and in compliance with all requirements of the protocol and TKL's Standard Operating Procedures.

7.1.4 Good Clinical Practices

This study will be conducted in accord with guidelines for the Protection of Human Subjects for research as outlined in 21 CFR Part 50, for Investigational New Drug Application (21 CFR Part 312) and, as appropriate, for Institutional Review Boards (21 CFR Part 56). If requested, copies of relevant standard operating procedures will be made available to the Sponsor for inspection on site.

7.2 Documentation of Data

The case report forms will be designed to identify each subject by subject number and/or subject entry number, and, where appropriate, subject's initials, the study material evaluated, and the reactions observed. Originals or copies of all case report forms, source documents, IRB documents (if required), correspondence, study reports, and all source data will be kept on hard-copy file for a minimum of five years from completion of the study. Storage is maintained at either a TKL Research, Inc. facility in a secured room accessible only to TKL employees, or at an offsite location which provides a secure environment with burglar/fire alarm systems, camera detection and controlled temperature and humidity. Documentation will be available for the Sponsor's review on the premises of TKL Research, Inc.

7.3 Monitoring of the Study

The Sponsor may make site visits during the study and may inspect all case report forms and other documentation directly associated with the study.

7.4 Final Report

At the conclusion of the study, the Sponsor will receive a final report including background data, study materials, tables of raw data and data summary, and an interpretation with discussion of results.

7.5 Investigator's Agreement

TKL Research, Inc. agrees to conduct the title study as provided in this protocol, in accordance with all government regulations and to make no changes without prior notification to the Sponsor except where a modification is deemed necessary to eliminate or reduce risk to human subjects.

SUBMITTED BY:

Maureen Damstra

Maureen Damstra, Clinical Research Coordinator
TKL Research, Inc.

3/28/00
Date

APPROVED BY:

J Frank Nash

J Frank Nash, Ph. D., Senior Scientist
The Procter & Gamble Company

04/09/00
Date